give much information. Successive records on the same case may give more.

12. The customary single recording of the blood-pressure in one position gives no information as to the gravity resisting function of the circulation.

PERNICIOUS ANEMIA: A STUDY OF ONE HUNDRED AND FORTY-EIGHT CASES.

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The study embraces a total of 148 cases discharged from the Cook County Hospital under the diagnosis of pernicious anemia, which may be divided into two main groups: (1) those in which the diagnosis was purely clinical, and (2) those in which the diagnosis was confirmed or corrected at autopsy. There were 22 of these latter. Of the other cases, 126 in number, 112 may be accepted, on the basis of the clinical study, as pernicious anemia; another group of 14 cases is made up of those which were discharged, with a question as to the diagnosis. Of the 112 cases accepted as clinically pernicious anemia, 26 will be discussed as a separate group, since they presented, as a major manifestation, the important group of symptoms denoting involvement of the spinal cord. There are therefore, 86 cases left to be studied as cases typical of pernicious anemia.

Certain features, however, may best be discussed with reference to their occurrence on the basis of the total figures. Of the total number of cases, 134 in number, clinically regarded as pernicious anemia, 94 occurred in males and 40 in females, an incidence of 70 per cent. and 30 per cent. respectively. Of the 134 cases, 67 died in the hospital, 67 left the hospital: some of them no better, many improved and a few recorded as worse and leaving at their own request. The number of histories actually studied was 161; nine of the patients had records of two periods in the hospital and two each had three histories. The histories used covered a period from 1912 to the present time. Seven of the patients were under thirty years of age; 31 were between thirty and forty; 39 were between forty and fifty; 36 between fifty and sixty; 35 over sixty. Only 6 of the cases occurred in negroes; evidently the incidence of the disease in negroes is low; the percentage occurrence here is slightly under 5; it is safe to assume that the percentage of negro patients in the County Hospital is at least twice this figure. So far as statements could be obtained the disease had lasted, prior to admission to the hospital, less than six months in 28 cases, between six months and two years in 40 cases and more than two years in 34 cases.

We will consider first the 86 cases, diagnosed as pernicious anemia, in which there were no cord symptoms or in which such symptoms were minor. A few symptoms were repeated with monotonous regularity. The symptoms of onset, as described upon the patient's admission to the hospital, may be listed as follows: Weakness, progressive in character, was mentioned 66 times; dyspnea, especially marked on exertion, 43 times; edema of the feet, in most cases worse at night, 34 times; gastric disturbances were frequent; vomiting, which occurred in 32 cases, was characterized by the absence of any regularity or relation to the taking of food; in some patients vomiting had occurred at rather long intervals and persisted for several days at a time; others would vomit "everything they ate" for weeks at a time, and others, now and then, without any apparent cause; in 10 of the cases it was stated that no blood had been vomited; in only 1 was there a history of bloody vomitus; and 20 patients expressly stated that no vomiting had occurred. Two reported themselves as very hungry; in 13 the appetite was good and 30 others made complaints of various degrees of absence of appetite. Sixteen complained of a fulness or dull pain in the abdomen; in 4 cases this was aggravated by eating. In 17 the bowels had been regular; in 17 there was constipation; in 12 diarrhea and in 4 an alternating constipation and diarrhea. Loss of weight was mentioned 26 times; in 24 of these a definite figure was given; the average loss of weight was thirty-two pounds; in 8 cases it had amounted to more than forty pounds. Dizziness was a symptom in 20 cases; palpitation of the heart in 16; headache in 13. Numbness, with or without coldness of the extremities, was an early symptom in 19 cases; cramps and shooting or dull pains in the legs were noted 6 times. The pallor was only mentioned 10 times, and in only 3 cases did the patient speak of the yellow color of the skin. Double vision had occurred once; other infrequent nervous symptoms were drowsiness, tinnitus, nervousness, irritability and insomnia. Only 3 patients gave a history of fainting. Epistaxis was mentioned 6 times; hemoptysis in 2 other cases. A sore-mouth occurred in only 4 cases. Fourteen complained of cough and 6 of night-sweats.

One patient stated that his mother had died of pernicious anemia; there was nothing of importance in the family or personal histories nor any evidence of relationship to past diseases.

On physical examination the "lemon yellow" color of the skin was noted 36 times; "jaundice," 8. Whether or not the yellowish color was incorrectly interpreted as "jaundice" cannot be said. In every instance the pallor of the skin, mucous membrane and scleræ was noted. Carious teeth were mentioned 32 times and pyorrhea 19; while atrophy of the lingual papillæ was only mentioned twice. It seems likely that the oral and lingual mucous membrane was not carefully examined. The cardiac findings were of special interest;

systolic murmurs were noted at the apex alone in 25 cases; at the base alone in 8 and at both base and apex, or over the entire precordium, in 21—a total of 54 cases. To these must be added 3 cases in which a presystolic murmur was described at the apex; another with a presystolic thrill and murmur and a systolic murmur at the apex; another with a diastolic murmur at the base (in which an autopsy one year later showed no organic cause for the murmur); another with a systolic at the apex and a diastolic along the left border of the sternum; a total of 60 cases which showed cardiac murmurs. The presence of a murmur may be regarded as one of the most constant findings of pernicious anemia. In this series it was present in 70 per cent. of the cases. Cardiac irregularities were uncommon—only 3 were described; these were probably of the type known as premature ventricular contractions. The cardiac outlines were recorded 36 times; in 28 of these the area of cardiac dulness was increased. Dilatation as a finding in pernicious anemia is equally as common as the presence of murmurs. The blood-pressure estimation varied from a systolic of 84 to one of 176; of 55 readings only 5 were above 150; 32 were below 115, 10 of these below 100. In view of the fact that the disease is one of adult life, it may be concluded that a low blood-pressure is the rule, and a blood-pressure higher than the normal for the age is an unusual finding in a case of essential anemia. The diastolic pressure varied from 40 to 90; of 50 readings, 35 were below 70; the average pulse-pressure was 53. We can regard the blood-pressure of pernicious anemia as characterized by a low systolic reading, a disproportionately low diastolic and an unusually high pulse-pressure.

The liver was palpable in 35 cases; 10 times it was stated to be as much as three finger-breadths below the costal arch; the spleen was palpated 19 times; general adenopathy was recorded but 4 times. Edema of the extremities was noted 23 times; extensive edema 4 times. The pulmonary findings were negligible; in 7 cases subcrepitant rales over both bases posteriorly were described; in 2 cases "coarse rales throughout the chest;" in another, dulness with increased tactile and vocal fremitus over both apices. A few cases presented the findings of old healed apical tuberculosis.

In 23 cases the temperature was never over 99; in 32 it usually ran from 99 to 100; in 12 from 100 to 101; in 8 over 101 at least once; this does not include some cases with terminal temperature; of 75 cases, fever was present at some time in 52. The pulse was frequently 100 or over in 29 cases. The pupils were noted as being normal in 77 cases; in 7 they reacted normally but showed irregularity or inequality. Only 2 of the patients had epistaxis while in the hospital. The reflexes were noted as normal in 57 cases; in 3 they were exaggerated; in 7 the patellar and Achilles reflexes were absent; in 1 other the patellar was absent on one side.

Sputum examinations were made in 10 cases; all were negative for tubercle bacilli. For the other laboratory findings, aside from the blood counts, we will give the figures from the total of cases diagnosed during life as pernicious anemia without qualification, 134 in number. The Wassermann test on the blood is recorded for 46 cases; 42 were negative, 3 were 4+ positive, another, 1+. The test on the spinal fluid was negative 14 times. Gastric analyses were recorded in 57 cases; 53 of these showed no free HCl; 1, a free HCl of 2; 2 others of 7; the other case showed so much blood that acidity could not be tested for; of the 56 cases tested, 29 showed a total acidity under 10, 21 between 10 and 20, and 6 over 20. In 93 per cent. of the cases examined the stomach contents showed no free HCl; the achylia is obviously an important clinical symptom of pernicious anemia. Of 53 urine examinations taken at random 37 showed a specific gravity of less than 1015; 24-hour specimens from 8 patients showed a total of more than 1500 c.c. in 7 instances; in the other the amount was 350 c.c. The urine was otherwise negative in 41 cases. Albumin was present without casts in 7 instances; with hyaline and granular casts in 2; a few hyaline casts were noted twice; a few red cells in the remaining case. We believe these conclusions are warranted: The usual urine of pernicious anemia is increased in amount and of a low specific gravity; albumin is not often found and the constant presence of albumin and casts makes the case questionable, speaks against the diagnosis of pernicious anemia and for the existence of a nephritis as the fundamental disease producing the anemia. Ophthalmoscopic examination was recorded 17 times; in 2 instances the eye-grounds were negative; in 6 there were hemorrhages; in 3 the disk was "hazy;" the eye-grounds were noted as pale 5 times; there was bilateral "beginning optic atrophy" once. In 45 cases examinations of feces were made; in 24 of these search was made for ova or parasites but none were found, and all the examinations were negative for pus and blood.

We come now to a consideration of the blood counts. The lowest erythrocyte count was 320,000. There were in all 6 patients with red counts below 500,000; 2 of these recovered sufficiently to leave the hospital. Thirty-six patients had erythrocyte counts below 1,000,000; 19 of these improved sufficiently to leave the hospital; thus the percentage of deaths in the hospital was 47. The patients with erythrocyte counts of 1,000,000 or above numbered 50; of these 14 died in the hospital, a mortality of 28 per cent. The prognosis is made decidedly worse as the red cells diminish. Only 8 of the cases had initial counts of more than 2,000,000; in this group there were 2 deaths; 1 occurred after a profuse hemorrhage from the nose and mouth; the second case had been admitted to the hospital with a history of hemorrhages from the nose, stomach and bowels; his color index was 0.5; no hemorrhages were noted in the hospital but he failed rapidly. The color-index was 1+ in 74 cases and below 1 in 12. Nucleated red cells were described in 31 cases.

The highest leukocyte count was 30,000; in this case there had been pain over the upper sternum for one month; this was intermittent and worse on exertion; there was swelling of the abdomen; hemorrhoids were present; there were nausea and vomiting, especially in the morning; the color-index was 0.83; this case was distinctly questionable. The next highest white count was 13,900; only 3 counts over 10,000 occurred; there were 41 counts below 5000, a percentage of 45, and 16 of 3000 or below; the lowest count was 1100. In 24 cases there was a distinct relative lymphocytosis; in 23 the differential white count was normal; in 39 it was not noted. Thus when a differential count was made a relative lymphocytosis was present in a majority. The conclusion seems justified that pernicious anemia is characterized by a low white count, with a tendency to a leukopenia and a relative lymphocytosis. Fourteen cases, or 58 per cent., of relative lymphocytosis occurred among the 36 cases in the group characterized by red counts of less than 1,000,000; 7, or 50 per cent., of these died. It seems that the appearance of this relative lymphocytosis is of grave prognostic import; only 2 of these 14 cases showed total counts over 6000; the condition really signifies an absolute decrease of the polymorphonuclears, which is significant of failure on the part of the blood-making organs to meet the constant and excessive demands on their function.

A few cases deserve special mention in our consideration of the blood counts:

F. G., aged thirty-two years, was in the hospital from June 1 to September 11, 1915. On admission his blood examination showed hemoglobin 22, erythrocytes 990,000, leukocytes 3150; all the pathologic forms of erythrocytes were present. August 30 examination showed hemoglobin 75, erythrocytes, 4,640,000, leukocytes 8200, and a few poikilocytes. He had been treated with dilute hydrochloric acid, sodium cacodylate and enemata of normal salt solution, 1 gallon every morning.

H. O., aged fifty-six years, was admitted to the hospital June 13, 1914. He was irrational and very sick. Blood examination showed 560,000 erythrocytes, 6200 leukocytes, color-index 2, small lymphocytes 44, large lymphocytes 10, polymorphonuclears 42. All forms of pathologic reds were present. She was discharged July 25, 1914, at which time the examination showed 80 per cent. hemoglobin, 4,040,000 erythrocytes and color-index 1. The stained specimen was normal. She was treated with Fowler's solution.

A somewhat similar case was that of W. C., aged forty-two years, admitted to the hospital May 6, 1916, and discharged July 3, 1916. On examination his blood showed hemoglobin 26, erythrocytes 792,000, leukocytes 4700, small lymphocytes 50, polymorphonuclears 50. On discharge his hemoglobin was 80, erythrocytes 4,032,000, leukocytes 4000, small lymphocytes 28, large lymphocytes 10, polymorphonuclears 48, eosinophiles 6, transitionals 7, myelocyte one, The treatment consisted of Fowler's solution and sodium cacodylate. In December of the same year he came under our observation at Mercy Hospital. He was once more in poor condition and died there a few days after an injection of neodiarsenol.

R. M., aged thirty-six years, was admitted to the hospital September 15, 1915, and discharged December 27, 1915. On admission his blood showed hemoglobin 15, erythrocytes 496,000, leukocytes 4100, small lymphocytes 56, large lymphocytes 2, polymorphonuclears 38, eosinophiles 2, one transitional and one myelocyte. All pathologic forms of erythrocytes were present. At discharge his hemoglobin was 60, erythrocytes 4,120,000, leukocytes 8000, small lymphocytes 12, large lymphocytes 3, polymorphonuclears 82, a few poikilocytes. The treatment consisted of dilute hydrochloric acid, sodium cacodylate, Fowler's solution and normal saline flushings, 1 gallon every other day. He was readmitted to the hospital the following summer and his fortune was not so good. He died in September. The autopsy report dated September 23, 1916, reads: "Lemon-yellow discoloration of the subcutaneous fatty tissues of the body; edema of the pannicular adiposis and the mediastinal fatty tissues and of the renal fatty capsules; marked systemic anemia; marked hyperplasia of the spleen; 'red' bone-marrow; marked fatty changes in the myocardium, liver and kidneys; dilatation of the mitral and tricuspid rings; fatty changes in the intima of the coat of the aorta; passive hyperemia of lungs and liver."

In estimating the results of treatment such experiences as these are of great value. In a disease characterized by remissions such as have just been described it is easy to be oversanguine about the results of any treatment which may be employed.

In the group of 26 cases characterized by the predominance of nervous symptoms there were 19 males and 7 females. Only one patient was under forty; evidently the spinal-cord lesions are more liable to occur in older patients. The usual development of the symptoms might be summarized as follows: After a period during which the patient suffered from various disturbances of sensation, with or without a weakness of the legs, out of proportion to the general symptoms, incoördination or ataxia would supervene. Five of the 26 cases had urinary incontinence and 4 more had both urinary and rectal loss of control. The paralysis of the lower extremities was noted as flaccid 4 times; in 5 cases there was a spastic paralysis. The ocular reflexes were normal 22 times; in 2 cases there were Argyll-Robertson pupils; in another the pupils were noted as sluggish; in the other the right pupil was irregular and did not react to light. The patellars were absent 12 times and exaggerated 9. There was a Babinski in 12 cases. An ankle-clonus was seen 3 times. In 3 cases all the reflexes, biceps, triceps, patellar and Achilles were exaggerated. The abdominal reflexes were absent 5 times. There was one case of impotence; one of an aggravated psychosis. In general the symptoms and physical findings pointed to a combined sclerosis; no case of true posterior sclerosis was seen. Among the 26 cases there were 14 deaths in the hospital. Only 3 of the 26 cases showed erythrocyte counts of less than 1,000,000 on admission; the leukocytes averaged 6630; there were only 4 cases with a lymphocytosis; in these the highest total leukocyte count was 4000.

We may infer that the predominance of the nervous symptoms renders the prognosis worse independently of the grade of the anemia. In 15 cases the blood Wassermann was negative; in 11 both blood and spinal fluid Wassermanns were negative. In 1 case there was a positive blood Wassermann with a negative spinal fluid. The spinal fluid was negative, except for a slight increase of pressure once, in all the 12 cases. The process in the cord must be a selective toxic degenerative process, not inflammatory and probably not syphilitic. The symptoms and signs of cord involvement without a positive spinal fluid call for a careful examination of the blood.

Of the 22 cases which went to autopsy 5 proved not to be pernicious anemia. These included (1) a case of Laennec's cirrhosis in which the clinical diagnosis had evidently been based on the blood findings in spite of the ascites. The blood findings were in the main those usually regarded as characteristic of primary anemia, namely, hemoglobin 26, erythrocytes 1,165,000, color-index 1.3. There were also nucleated reds of all sizes. The leukocyte count was 11,200 and the differential normal. (2) Aortic stenosis and regurgitation, with a question about pernicious anemia because of the blood findings. These were hemoglobin 26, erythrocytes 1,340,000, color-index 1, leukocytes 3750. Differential count showed a slight polymorphonuclear relative increase. The autopsy showed the aortic lesions and a moderate interstitial nephritis. The characteristic findings of pernicious anemia were not present. (3) A case of streptococcic septicemia. A poor history had been obtained from this patient. The hemoglobin was 42, erythrocytes 1,916,000, color-index 1+, leukocytes 2850; nucleated reds were not recorded. The autopsy showed an acute serofibrinous pericarditis, embolic abscesses of the bowel and a "large septic spleen." (4) This patient gave a history of sudden onset two weeks previous to admission; there was fever, with chills, sweats, weakness, dizziness and nervousness. The ophthalmoscope showed small flame-shaped hemorrhages; there were inconstant rales in the left axilla about the sixth interspace. Gastric analysis showed no free HCl; total acidity 15. The feces were negative for pus, ova, parasites or blood. Blood examination showed hemoglobin 21, erythrocytes 1,208,000, color-index 1, leukocytes 4450, small lymphocytes 57, large lymphocytes 23, polymorphonuclears 13, basophils 1, myelocytes 6 and many nucleated reds. This case is particularly interesting because it simulates so closely the findings of an aplastic anemia. The onset described in the history is somewhat inconsistent with pernicious anemia, but it is often difficult to get an accurate history from patients at the County Hospital. Aside from this the features which made the case one not to be regarded as typical of an essential anemia were the color-index just about normal and the predominance of lymphocytes, even though blood formation was still active, as shown by the presence of myelocytes and nucleated reds. Yet the blood findings in the absence of definite findings of another disease, the retinal hemorrhages, and the achylia made the diagnosis of pernicious anemia a logical one, and the result emphasizes what is perhaps the thing most to be remembered about pernicious anemia: the disease can be exactly simulated by the anemia dependent on some definite etiologic factor, such as carcinoma or tuberculosis. In this case the autopsy showed; "Nodular fibrocaseous tuberculosis of the tracheal, bronchial, biliary, retroperitoneal and mesenteric lymph nodes; bilateral fibrocaseous and nodular pulmonary tuberculosis; nodular tuberculosis of the kidneys, liver and spleen, multiple hemorrhages into the epicardium and lining of the stomach; moderate bilateral serosanguineous pleuritis." (5) This case presented the symptoms of weakness, fainting and edema of the feet, palpitation and loss of weight and pain in the back in the lumbar region of both sides. There were no gastric disturbances. The patient was fifty-two years old. There was dilatation of the heart. The liver was palpable. Reflexes and sensation were normal, although the "gait was uncertain." Spinal fluid was negative. Wassermann was negative on the blood and spinal fluid. Blood-pressure was 120 systolic and 70 diastolic. Urine was negative. Blood examination showed hemoglobin 35, erythrocytes 1,770,000, color-index 1.4, leukocytes 12,400. There is a note on the history: "The findings make quite certain the diagnosis of pernicious anemia." The feces were not examined. The autopsy disclosed an "annular carcinoma of the ascending colon." The pathologic conditions characteristic of pernicious anemia were not present. The pain in the back should not have been ignored and it may be emphasized that the leukocytosis should not have been disregarded.

Of the remaining 17 cases 9 went to autopsy as pernicious anemia alone. This diagnosis was confirmed in all without essential modification. In one case an acute pericarditis was found, probably terminal. In another the patient had evidently died of an acute pulmonary edema. The protocol of G. F., who died at the age of twenty-two years, may be taken as representative of the group: "Systemic anemia; marked fatty changes in liver, myocardium and kidneys; fatty degeneration of the lining of the aorta; 'red' bone-marrow; anasarca; passive hyperemia and edema of the lungs; moderate hyperplasia of the spleen; atrophic gastritis; left-sided fibrous pleuritis; disseminated petechial hemorrhages in the gastric mucosa and the mucous membrane of the urinary bladder." Two cases were diagnosed pernicious anemia and lobar pneumonia; one pernicious anemia and chronic nephritis; one pernicious anemia and parotitis; all of these were essentially confirmed; 2 cases were both diagnosed pernicious anemia and organic heart disease. In both the diagnosis of pernicious anemia was correct; in 1 there was a chronic parenchymatous (large white) kidney but no heart disease other than the "marked fatty changes in the myocardium;" in the other the only cardiac changes noted were "dilatation of the mitral ring" and "fatty changes in the myocardium."

In 10 of the 15 cases the red count was below 1,000,000 on admission; two of the counts were below 500,000; the highest count was 2,000,000. The color-index was over 1 in all of the 15. The highest leukocyte count was 10,000 and the lowest 1300; the average was 4530. Seven, or 58 per cent. of the cases in which a differential leukocyte count was made showed a relative lymphocytosis. In one case the total count was 4900, with a lymphocyte count of 88 per cent. In 12 of the 15 cases nucleated reds were found. Our views of the blood findings, commonly accepted as characteristic of pernicious anemia, were confirmed by these autopsies; the cases which went to autopsy, in which the pathology of pernicious anemia was found, had conformed clinically most closely to the accepted standards of pernicious anemia. Of the 15 patients 12 were men; 2 were under thirty years of age (one was only twenty-two), 6 between thirty and forty, 5 between fifty and sixty and 2 over sixty. All were white.

An apical systolic murmur was found in 3 cases, basal systolic in 4 and a murmur systolic in time, both at base and apex, in 2. In 1 case there were described a presystolic thrill and murmur at the apex; no valvular disease was found at autopsy. In another case the history contained a record of a presystolic thrill at the apex, a presystolic murmur at the apex and systolic and diastolic murmurs at the base. Duroziez's phenomenon was also present. *The autopsy protocol stated that the cardiac valves were normal.* The maximum systolic blood-pressure was 138 and the minimum 90; of 11 readings the systolic pressure was below 115 in 8; the average pulse-pressure was 50. The spleen was palpable in 5 cases. The urinary findings also corresponded to those obtained in the cases observed only clinically; the specific gravity was low in 10 cases; otherwise the findings in these were negative; in 1 there was a trace of albumin; in 1, without albumin, a few finely granular casts; in 2 without albumin, a few hyaline casts. Only 1, the case diagnosed as pernicious anemia and nephritis, showed albumin and hyaline and granular casts. The patient, in whom the chronic parenchymatous nephritis was later found, had shown nothing in her urine except some finely granular casts. The blood-pressure in this case was not taken. In the autopsy reports atrophy of the gastric mucosa was mentioned only 3 times. The spleen was hyperplastic in 10 cases.

Two cases went to autopsy with a diagnosis of "suspected abdominal malignancy;" in 1 case the color-index was high; the highest leukocyte count was 6800; there were no nucleated erythrocytes; in the other case no blood counts were recorded, as the case apparently was regarded as certainly one of malignancy. In both cases the characteristic findings of pernicious anemia were present.

Fifteen cases in another group were discharged as pernicious anemia but with some qualification. Of these 10 were males; the youngest patient was ten; 4 others were under thirty; 5 between thirty and forty and 5 over forty. There is a notable variation here from the age incidence in the cases of true pernicious anemia. In the latter the proportion of patients over 40 was distinctly greater. Six of the 15 patients died in the hospital.

This group can best be considered in several subgroups:

Two cases of pernicious anemia with nephritis. In one case the urine contained much albumin, hyaline and granular casts and red blood cells; in the other there was generalized edema, with dyspnea, headache and insomnia; the color was waxy; there was evidence of fluid in both pleural cavities; the urine was albuminous, containing hyaline and granular casts. The respective blood counts were hemoglobin 36, erythrocytes 1,690,000, color-index 1.4, leukocytes 6400, differential count normal; no nucleated reds. Hemoglobin 15, erythrocytes 1,560,000, color-index, 0.4, leukocytes 26,200. Obviously the latter may be dismissed as nephritis, with severe secondary anemia.

Three cases with hemorrhages: The first, a man aged thirty-seven years, had epistaxis and hemorrhages from the bowels; the gums bled easily; there were also hemorrhages from the ear. The blood count showed hemoglobin 22, erythrocytes 1,165,000, color-index about 1, leukocytes 12,000, with 86 per cent. polymorphonuclears. The history is that of a purpura hemorrhagica; the findings are those of a secondary anemia.

The second, a man, aged forty-five years, who complained of loss of blood during defecation, persisting for some time and growing worse, until at the time of entrance to the hospital he was passing an ounce or two with every movement of the bowels. No hemorrhoids were found. The blood count was hemoglobin 37, erythrocytes 1,808,000, color-index 1.1, leukocytes 3600, with a relative lymphocytosis, small lymphocytes 38 per cent. and large 15 per cent. There was poikilocytosis but no nucleated reds were found.

The third, a man, aged thirty-six years, with hemoptysis and severe nose-bleed. The day before his death it was noted that he had a "profuse hemorrhage from mouth and nose." The blood count shortly before his death was hemoglobin 25, erythrocytes 960,000, color-index 1.3, leukocytes 21,300; polymorphonuclears 84 per cent.; a few nucleated reds. Again the findings are not typical of pernicious anemia.

Four cases of pernicious anemia with heart disease. The first showed general anasarca and dyspnea, with marked evidence of ascites; there was a systolic blow at the apex, with a gallop rhythm. The blood count was hemoglobin 10, erythrocytes 742,000, color-index 0.7, leukocytes 4800, polymorphonuclears 75, myeloblast 1.

The second patient had mitral insufficiency with healed apical tuberculosis. The blood-count on admission was hemoglobin 18, erythrocytes 896,000, color-index 1.2, leukocytes 2550; there was a relative lymphocytosis, these cells making 50 per cent. After transfusions the patient improved very much, leaving the hospital ten weeks after admission with a red count of 2,608,000 and a hemoglobin of 45. The dilated heart, the mitral murmur and the evidence of old tuberculosis fail to convince one that this was not a case of pernicious anemia, with cardiac findings, such as have been discussed. There was, moreover, no record of generalized edema nor of cardiac dyspnea.

The third was a case diagnosed as pernicious anemia, with mitral stenosis, regurgitation and aortitis. There was a history of rheumatism and symptoms of cardiac incompetency for eighteen months. There were moist rales over the bases of the lungs. Blood count was hemoglobin 17, erythrocytes 1,244,000, color-index 0.8, leukocytes 6800, polymorphonuclears 77 per cent.; no nucleated reds.

The fourth case was characterized by generalized anasarca, dyspnea and a tendency to nose-bleed; the heart was very irregular. The blood count was hemoglobin 23, erythrocytes 719,000, leukocytes 8000, color-index, 1.6, differential normal; very few nucleated reds. The urine was negative. The feces contained no blood, but did show a great many of the parasites known as trichomonas intestinalis, an organism usually regarded as non-pathogenic.

Two cases with a definite focus of infection. The first is one of the most interesting cases of the series. The patient, a man, aged fifty-four years, entered the hospital May 6, 1918. He presented the usual symptoms of pernicious anemia, but in addition complained of a pain in the left leg, deep in the bone, which had been present for six years. The blood count on admission showed hemoglobin 45, erythrocytes 1,190,000, color-index 1.9, leukocytes 3200, poikilocytosis and small lymphocytes 78 per cent., large lymphocytes 6 per cent., polymorphonuclears 14 per cent., eosinophils 2 per cent., 1 normoblast was found. Four weeks later his erythrocytes were 770,000. He was transfused June 30, 600 c.c. of blood being given. On July 15, his blood count was hemoglobin 29, erythrocytes 1,370,000, color-index 1.08, leukocytes 6650. One week later an incision was made over the upper one-third of the left tibia through the periosteum and 4 ounces of pus were discharged. Eight days after the operation the hemoglobin was 45, erythrocytes 2,220,000, color-index 1.03, leukocytes 7750. Two weeks after the transfusion his hemoglobin had increased from 18 to 29, his erythrocytes from

770,000 to 1,370,000; eight days after the successful drainage of a subperiosteal abscess the hemoglobin had increased from 29 to 45 and the erythrocytes from 1,370,000 to 2,220,000. He was discharged September 9 with a hemoglobin of 63, erythrocytes 3,280,000 a color-index of 1 and a leukocyte count of 6300.

The second was the case of a boy, aged seventeen years, who had been operated on for an osteomyelitis of the left femur ten months previously. For a while he ran a temperature of 104°. Chronic osteomyelitis was found on Roentgen-ray examination but no local symptoms appeared and no operation was done. No other focus of infection was found. His blood count was hemoglobin 27, erythrocytes 725,000, color-index 1.92, leukocytes 2900, small lymphocytes 44 per cent., large lymphocytes 10 per cent., polymorphonuclears 44 per cent., eosinophils 1 per cent., transitionals 2 per cent. This patient died after a transfusion.

The question of diagnosis in this instance must be regarded as unsettled.

Of the 4 cases remaining one was probably a case of sprue and so noted. He had been a patient in a U. S. Army hospital in the Philippines. For two years he had suffered with stomatitis and diarrhea. The stools were frothy, whitish, very foul and contained no blood. The blood count, at the lowest, showed hemoglobin 20, erythrocytes 990,000, leukocytes 4000; no nucleated reds and a normal differential white count.

The second was the case of a man in whom the Roentgen ray discovered a lesion at the pylorus. The blood examination showed the findings usual in secondary anemia except for a high color index and a white count of only 5400, once as low as 2800.

The third case was one of "old pulmonary fibrosis, with an advanced secondary anemia" (a red corpuscle count of 1,480,000) and a high color-index.

The fourth was a case originally diagnosed as Banti's disease and discharged from the hospital October 26, 1915, with that diagnosis. She returned in December of the same year and died two months later of pneumonia. She entered the hospital the first time, with a marked ascites. A large spleen was palpated and the patient stated that she had known of this enlargement for twenty years. She was tapped three times. The specific gravity of the fluid was 1006 to 1010. Her lowest blood count was hemoglobin 25, erythrocytes 3,000,000, color-index, 0.5, leukocytes 3400. At the time of the second admission the blood examination showed hemoglobin 5, erythrocytes 870,000, leukocytes 34,000, polymorphonuclears 87 per cent.; all forms of nucleated reds. The most plausible theory about this case is that some of the findings of pernicious anemia (particularly the presence of nucleated erythrocytes) had developed on the basis of a long-standing secondary anemia. The original diagnosis of Banti's disease was probably correct.

In summarizing the last group of cases we find that in only 2 cases was the spleen palpable. One of these cases was the one originally diagnosed as Banti's disease; in 10 cases it was expressly stated that the spleen was not palpable. In 9 cases the color-index was above 1. There was a leukocytosis of more than 10,000 in 3 cases. In no case were the nucleated forms of the red corpuscles easily found. In 8 cases none were found and in the others they were very rare. In only 3 of the cases, or 20 per cent., did the lymphocytes exceed the polymorphonuclears. In the cases demonstrated at autopsy as pernicious anemia 43.7 per cent. showed relative lymphocytosis. In 2 of these 3 cases there were no nucleated reds; the third was the case of suppurative periostitis already described, which showed a high index, a relative lymphocytosis and very few normoblasts. As a general conclusion we may say that these findings warrant the opinion that great reserve should be exercised about making a diagnosis of pernicious anemia when all the characteristic blood findings are not present. In this type of case search for a definite etiologic factor is most urgent.

It would be a thankless task to attempt a review of the medicinal therapy, but we are interested in the use of human blood as a therapeutic procedure. There were in all records of 30 injections of human blood in 19 cases; 26 of these were intravenous transfusions with citrated blood in 16 patients; 3 were subcutaneous injections of whole blood, in 2 patients, and there was one subcutaneous injection of defibrinated blood.

In the last case 200 c.c. of defibrinated blood were injected subcutaneously, without reaction or result. In two cases whole blood was used subcutaneously. In one 20 c.c. of whole blood were injected without reaction or result. In the second one injection of 30 c.c. was given, with a slight reaction and no therapeutic effect. Four days later a second injection of 60 c.c. was given. Three hours after the injection the patient had a chill lasting twenty minutes: the condition improved but the pulse remained rapid and weak. Four days after the injection the temperature went to 102.6°. The next day evidence of suppuration was discovered in the buttock into which the injection had been made. Four days later the patient died. Death is attributable to the injection of blood only indirectly; it was not the result of a reaction but of an infection which the already debilitated patient could not stand.

Twenty-six intravenous injections of blood with sodium citrate were given to 16 patients; 2 of these were of small amounts, 10 c.c. to each of two patients. There was no reaction in either case and no benefit was apparent. The other transfusions varied in amount from 200 to 600 c.c. Three of these were done at Wesley Hospital on a patient afterward admitted to the County. In 4 of these no improvement is noted on the chart; after 17 of the transfusions distinct improvement was noted. We may cite 3 cases: the first, with a hemoglobin of 16 and a red count of 888,000, was transfused the first time September 24, 1916; three days later the blood examination showed hemoglobin 16, erythrocytes 1,536,000. The count fell to 808,000 on October 2; on October 3, another transfusion was done; on October 4, the count was 1,840,000; each transfusion was followed by an increased leukocyte count; following the second transfusion improvement was steady and the patient, much better, was discharged November 21.

In the second case the red count, August 5, 1918, was 1,050,000, with a hemoglobin of 30 and a leukocyte count of 2050. Transfusion was done on the seventh, and nine days later the blood examination showed hemoglobin 50, erythrocytes 4,070,000, leukocytes 4100. The patient, in good condition, left the hospital September 9.

A third case after the first transfusion showed a rise in the erythrocytes from 990,000 to 1,300,000; after the second, the hemoglobin rose from 25 to 35, the erythrocytes from 990,000 to 1,300,000; after the third the hemoglobin was unchanged at 30; the erythrocytes rose from 1,700,000 to 2,350,000. This patient did not continue to do well. A splenectomy was advised but refused; the patient shortly afterward was taken home in poor condition against our advice. There were 11 patients in this group showing improvement after transfusion; prior to the first transfusion the highest erythrocyte count was 1,200,000; only 3 patients had more than 1,000,000 erythrocytes; 8 of the 11 left the hospital improved (one improved after the transfusion, but much more rapidly after a collection of pus was evacuated, as mentioned elsewhere), 1 left the hospital in poor condition and 2 died in the hospital; one of these latter, shortly before her death, had an erythrocyte count of 3,800,000 and a hemoglobin percentage of 75; it had not been deemed necessary to transfuse her for four months; she died of complications incident to combined cord degeneration. We may say that of the 11 cases 9 showed marked improvement in the blood condition.

Three deaths occurred shortly after transfusion; in one case the transfusion was carried out as a measure of last resort in a moribund patient; there was no typical reaction and the death cannot be charged to the transfusion. In 1 case while the transfusion was in progress the patient complained of "dizziness and faintness, then became dyspneic, was nauseated and tried to vomit; there was headache and a clammy perspiration broke out; the transfusion was stopped. One-half hour later a severe chill occurred, lasting fifteen minutes; two hours later an attack of severe abdominal pain, dyspnea, pulse imperceptible; death occurred one-half hour later." The other fatal reaction took practically the same course. There were in all six severe reactions and three mild ones; seven of the transfusions were followed by no reaction.

There is a record of one splenectomy in the series; the operation was done after the patient had been in the hospital for three months and had made a notable gain; the patient was discharged in good condition one month after operation.

In reviewing the results of this study, we find:

1. The clinical complex known as pernicious anemia presents certain characteristic blood findings, particularly the high color-index, the presence of many large erythrocytes and of nucleated red cells, especially megaloblasts, and a tendency to a leukopenia, with a relative lymphocytosis; the clinical symptoms, though secondary in importance from the standpoint of diagnosis, are yet distinct and definite. The progressive weakness, the gastric disturbances; the dyspnea, pallor, the cardiac findings and the edema of the feet are the most typical and constant findings.

2. Though pernicious anemia has its own characteristic diagnostic findings these may be simulated closely by anemias resulting from various diseases; in fact, the blood picture of pernicious anemia may be presented exactly as the result of some definite septic, toxic or malignant condition. The diagnosis should rest not on the blood findings alone nor on the blood findings and symptomatology, but on these two features in the absence of any discoverable cause for the anemia.

3. The disease is more common in males and is most frequent in the fourth and fifth decades of life.

4. The cardiac symptoms and physical findings (the murmurs and the dilatation of the heart) are so constant as to be looked upon as among the most common symptoms of the disease. Anatomically valvular disease is not a part of pernicious anemia; the cardiac findings are the result of myocardial weakness and relative insufficiency. Ascites and anasarca are not symptoms of pernicious anemia though there is a possibility that they may result from cardiac incompetency, this event is so unusual that their presence demands explanation.

5. The systolic blood-pressure is almost never above normal but tends to be below the lower limit of normal; the diastolic pressure is disproportionately low and the pulse-pressure high.

6. The urine is usually of a fairly low specific gravity, rather increased in quantity, and rarely contains albumin. The presence of albumin is not to be accepted as a usual finding in pernicious anemia; its presence with casts means nephritis, which may be the cause of the anemia rather than the effect.

7. Pernicious anemia is characterized by an irregular temperature, which is not often above 101°; there are often recessions to normal of variable duration.

8. Achylia gastrica is so much the rule that the presence of free HCl may justifiably raise a doubt as to the diagnosis.

9. The Wassermann reaction occurs infrequently in pernicious anemia. In 46 cases there was a percentage incidence of 6.5; the general run of cases in a large charity hospital would probably

show a higher percentage. It is possible that certain changes in the blood incident to the disease interfere with the reaction.

10. The gradual decrease in the leukocyte count, especially in the relative and absolute number of polymorphonuclears, is of serious prognostic import. The diagnosis of pernicious anemia should be made with the utmost reserve in the presence of a leukocytosis.

11. The negative spinal fluid tests in the presence of well-established cord disease point to a toxic degenerative process in the cord rather than an inflammatory process. Disease of the cord, with pernicious anemia, usually means an involvement of the lateral and posterior columns, a combined cord lesion. The presence of evidences of cord disease is of unfavorable prognostic import; the prognosis in these cases is grave, out of proportion to the blood findings as compared to the cases not so complicated. These patients are less likely to live long enough to develop advanced grades of anemia.

12. Transfusion of blood will not cure but will often prolong the patient's life. The severe reactions which occurred in this series were likely the result of imperfect technic; the procedure has really been developed from its inception in the years covered by this study; transfusions are now being done with a much lower percentage of reaction. Yet the experiences noted here may have a valuable lesson for us. The transfusion of citrated blood is a simple procedure but not a harmless one. Before the operation is undertaken the bloods of donor and patient must be demonstrated to be compatible by an acceptable and approved technic.